

1841

16.11.60 FARB

3-AMINOBENZISOXAZOLES

Germ. 1,129,488 clg. (Non-Con) 16.11.60 (Germ.)
Farbenfab. Bayer A.G.

1-Aminobenzisoxazoles, having sedative and analgesic prop., are obtained simply and in good yield by heating an opt. sulfide, salicylic acid-(amidoxime-O-carboxylic acid ethyl ester) at 100-190°C. An inert suspension agent such as paraffin oil may be used and the heating is pref. effected in vacuo under N₂. The reaction product may be purified by crystallization or high vacuum distillation. In an example, 30 g. 5-chloro-salicylic acid-(amidoxime-O-carboxylic acid ethyl ester) (prepared from 5-chlorosalicylic acid-amidoxime and chloroformic acid ethyl ester, are cyclized to give 12.7 g. (60% of theory) of 5-chloro-3-amino-benzisoxazole. Similarly, 5-methyl-salicylic acid-(amidoxime-O-carboxylic acid ethyl ester) is cyclized to 5-methyl-3-amino-benzisoxazole.

1842

6.12.60 FARB

POLYHALOCYCLOPENTENES

Bel. 611,79 clg. 6.12.60 (Germ.)
Farbenfab. Bayer A.G.

Subst. polyhalo-cyclopentenes have internal or systemic therapeutic activity as fungicides; esp. against pathogenic microbes of withering diseases. They have general formula shown (wherein X is F, Cl, Br or I; R is alkyl, cycloalkyl or alicyclic group opt. subst'd. by halogen or other heteroatoms; and Y is R, X or H). Preferred cpds. are obt'd. by reaction of alkyl-, dialkyl-, trialkyl-, cycloalkyl-, di-cycloalkyl and tricycloalkyl-polyhalo-cyclopentenes with Cl₂ or Br₂.

Particularly active cpds. are those where the H atoms of the alkyl, cycloalkyl or alicyclic groups are completely or partially replaced by halogen and these cpds. may be prepared by process of French P. 1,276,891 (Belgian P. 598,169).

1843

19.12.60 FARB

N-GUANIDINOALKYL-AZABICYCLO-OCTANE OR NONANE

Bel. 608905 clg. 19.12.60 (Germ.)
Farbenfab. Bayer A.G.

new blood pressure lowering agents which have not the disadvantage of ganglion-blocking secondary effect are cpds. of the general formula shown



(wherein R is H or 1-3 C alkyl; R' is H or 1-4C alkyl; R'' is H, alkyl or alkenyl contng. 1-4C; Z is 2-5C alkyne; n is 1 or 2) as well as acid addition and quaternary salts thereof with non-toxic cpds. In an Example, 31.5 g. of n-(2-aminoethyl)-3-aza-bicyclo-(3:2:2)-nonane are refluxed for 2 hrs. in 100 cc. of alcohol and 10 cc. of water together with 27 g. of 6-methyl-isothiourea sulphate. After cooling the product is filtered, and after recrystallization in water there is obtained 45 g. of N-(2-guanimodethyl)-3-aza-bicyclo-(3:2:2)-nonane monosulphate. The starting material may

be obt'd. by heating 35 g. of 3-aza-bicyclo-(3:2:2)-nonane (itself prep'd. by removing ammonia from 1:4-bis-aminomethyl-cyclohexane using aluminium oxide catalyst in gas phase at 350°C) together with 13.5 g. of glycolic nitrile in 200 cc. of alcohol and 50 cc. of water to give 35.7 g. of N-cyanomethyl-3-aza-bicyclo-(3:2:2)-nonane which is reduced with lithium aluminium hydride in ether soin. at -5°C.

Best Available Copy

50

KINGDOM OF BELGIUM
No. 611.179

MINISTRY OF ECONOMIC AFFAIRS AND ENERGY
PATENT

The Minister of Economic Affairs and Energy,

Having regard to the law on patents of 24 May 1854;

Having regard to the Union Convention for the Protection of Industrial Property;

Having regard to the minutes drawn up on 6 December 1961 at 2.30 p.m. at the office of the clerk of the Provincial government of Brabant;

DECIDES:

Article 1 – The company called: FARBNFABRIKEN BAYER AKTIENGESELLSCHAFT, at Leverkusen-Bayerwerk (Germany), represented by Mr J. Bede in Brussels, is granted

a patent for: Fungicides with an internal therapeutic activity (Inventors, Messrs H. von Brachel and V. Flück), which it declares to have been the subject of a patent application filed in Germany (Federal Republic) on 6 December 1960.

Article 2 – *This patent is granted thereto without preliminary examination, at its risk, with no guarantee either of the reality, novelty or merit of the invention, or the accuracy of the description, and without prejudice to the right of third parties.*

Attached to this decision will be one copy of the specification of the invention (descriptive statement and possibly drawings) signed by the interested party and filed in support of its patent application.

Brussels, 6 June 1962

BY SPECIAL AUTHORITY

The Director General
(Signature)

J. HAMELS

The Company called: FARBENFABRIKEN BAYER A.G.
at Leverkusen-Bayerwerk (Germany)

Fungicides with an internal therapeutic activity.

C.I. Patent application of the Federal Republic of Germany
F32 707 IVa/451 filed on 6 December 1960.

Inventors: Hanswilli von Brachel and Victor Flück.

It has just been discovered that substituted polyhalogen-cyclopentenes, surprisingly, have an internal or systemic therapeutic activity as fungicides, particularly against pathogenic microbes in diseases of wilt, which, as is known, are unable to be controlled, or only with great difficulty, by common commercial fungicides.

The activity of substituted cyclopentenes as systemic fungicides is all the more surprising since these halogenated compounds are nearly insoluble in aqueous media and consequently their absorption by plants was not foreseeable.? [illegible]

With the substituted polyhalogen-cyclopentenes to be used according to the invention, one is dealing with compounds? [illegible] with a general formula:

[see figure]

in which X represents fluorine, chlorine, bromine or iodine, R an alkyl, cycloalkyl or araliphatic residue possibly substituted by a halogen or other heteroatoms, whereas Y represents R, X or hydrogen.

The polyhalogen-cyclopentenes to be used according to the invention can be prepared by various processes. The preferred compounds are those which are obtained by reaction of alkyl-, dialkyl-, trialkyl-, cycloalkyl-, dicycloalkyl- and tricycloalkyl-polyhalogen-cyclopentadienes with chlorine or bromine. Polyhalogen-cyclopentenes in which the hydrogen of the alkyl, cycloalkyl or aralkyl groups is partially or totally replaced by halogen have proved particularly active. Preparation of these compounds takes place preferably according to the procedure of French patent 1.276.891 of 14.12.60 (Belgian patent 5???.169? of 14.12.??)

As polyhalogen-cyclopentadienes whose products of chlorination or bromination? are especially used as fungicides, we will mention for example: ethyl-pentachloro-cyclopentadiene, isopropyl-pentachloro-cyclopentadiene, n-butyl-pentachloro-cyclopentadiene, n-decyl-pentachloro-cyclopentadiene, cyclohexyl-pentachloro-cyclopentadiene, di-n-propyl-tetrachloro-cyclopentadiene, ethyl-propyl-tetrachloro-cyclopentadiene, di-isobutyl-tetrachloro-cyclopentadiene, triethyl-trichloro-cyclopentadiene, ethyl-penta-bromo-cyclopentadiene, n-butyl-pentachromo-cyclopentadiene, di-n-butyl-tetrabromo-cyclopentadiene, ? [illegible] chloro-cyclopentadiene, (3-oxa?.....cyclopentadiene?, pentachloro-cyclopenta?.....?, phenoxyethyl-pentachlorocyclopentadiene, butyl-difluoro-trichloro-cyclopentadiene and ethyl-tetrachloro-cyclopentadiene.

The fungicides to be used according to the invention have many advantages compared with commercial fungicides. Thus, they are subject to less influence from the weather, because they are absorbed by the plant and are not removed by washing like fungicides which are just sprayed onto the surface of the plant. Furthermore, they reach every part of the plant and consequently also each new shoot, given that they have the ability to move in the sap flow in the plant.

They are consequently particularly active in the case of diseases caused by vascular parasites, such as for example in diseases of wilt where effective control was not possible up to now. The pathogenic microorganisms of these diseases of wilt, fusaria and verticillia, penetrate by the roots into the vessels, develop there and consequently their metabolic products lead, through the sap flow in the plant, to poisoning phenomena such as yellowing of the leaves, necrosis of the stem and leaves, inhibition of growth and in severe cases the death of the plant.

Detection of the systemic activity of substituted polyhalogen-cyclopentenes to be used according to the invention can be carried out as follows: tomato plants are put for 5 to 6 days in Knop & Hoagland A-Z nutrient solution and are then left for 10 days in Knop & Hoagland nutrient solution with 0.005% of the active ingredient described in example A. The roots are then cut approximately above the neck of the root and the shoots are again put in nutrient solution. After they have again produced roots, they are infested as described in example 1. The attack quotient of the plants thus treated amounts to 6?% of that of the control plants treated with pure nutrient solution (put as 100%) and the attack quotient of the unaffected plants amounts to 0%.

The method of action of the fungicides to be used according to the invention is not exactly known. Given that only limited effects are noted in vitro, it is possible that they change the predisposition of the plants (immunisation) so that the fungus no longer has the power to attack them. Another possibility however is conversion of the active ingredients in the plant.

Due to their lasting action and their specific method of action, substituted polyhalogen-cyclopentenes provide new means for controlling pathogenic diseases in plants. Thus, young plants, before transplanting in an infested medium, are immunised by appropriate pretreatment.

Such immunisation can be carried out in particular by placing the plants, for example young tomato plants, 6 to 10 days before they are transplanted with the top part of the root in a preparation solution, or by keeping for example carnation cuttings in a sand impregnated with the preparations. Preferably the plants, when put into position, are once again treated with the preparation, for example in the form of granulate or a wettable powder. Or they can be watered directly after planting with highly diluted aqueous emulsions of the active ingredients. The compounds to be used according to the invention thus allow long-lasting protection of the plants.

Another possibility consists finally of use on older plants which are already threatened with attack. For example, during the sporadic appearance of signs of wilt, healthy plants will be protected in the surroundings of the sick plants by means of the preparations.

The following examples will illustrate the invention further.

Example 1

The experimental process and the assessment were carried out according to the method of Diamond et al. 1952, Bull. 557, Connecticut Agric. Exp. Stat. New Haven, on tomatoes.

The application is altered however as follows: 100 cm³ is applied each time per plant 2 to 3 times before the infection at an interval of 96 hours, or twice before the infection and 5 + 10 days after the infection to the roots. The chemical products are moreover buried under the soil in the state of wettable powder and administered to the plants before the infection. The assessment took place 20 to 25 days after the infection. The latter was changed however as follows: instead of a suspension of mycelium and spores, a solid *Fusarium oxysporum* inoculum was used. The fungus is cultured for 6 days on a mixture of sand: cornflour of 90: 90:10 [sic]. 200 cm³ of

this mixture is put into each of the 500 cm³ Erlenmeyer flasks, and 40 cm³ of distilled water is added. With this inoculum and the soil a 1:10 mixture is prepared and the plants to be infected are potted up, with 450 cm³ of soil: inoculum per pot. The infected plants are put in a greenhouse at 25°C, with a relative humidity of air of 60 to 70%. They are given supplementary illumination during the winter months.

The substituted polyhalogen-cyclopentenes used are obtained by passing chlorine with irradiation by means of a UV lamp or with heating at 85-100°C in the presence of 1 to 3% of azo-bis-isobutyronitrile, until the desired quantity of chlorine is absorbed. In particular the following compounds mentioned in the table are used:

Description	Initial diene	Approximate global formula of chlor. prod.
A	ethyl-pentachloro-cyclopentadiene	C ₅ Cl ₇ C ₂ H ₄ Cl
B	n-propyl-penta-chloro-cyclopentadiene	C ₅ Cl ₇ C ₃ H ₄ Cl ₃
C	n-butyl-penta-chloro-cyclopentadiene	C ₅ Cl ₇ nC ₄ H ₅ Cl ₄
D	isopropyl-hepta-chloro-cyclopentadiene	C ₅ Cl ₇ -iso-C ₃ H ₃ Cl ₄

Compounds A and D are previously dissolved in the tenfold quantity of a 10% solution of an oxyethylated nonylphenol, having a molecular weight of 468, in acetone, then diluted with water up to the watering quantity applied. 1 part of emulsifier solution is used per 100 parts of water.

Preparation	Concentration for each watering	Attack quotient as % of attack
A	0.0125%	1
B	0.0125%	1.7
C	0.0125%	1.7
D	0.0125%	0
controls	-	100

Example 2

0.06 g of active ingredient A is applied with 10 g of talc per pot with 450 cm³ of soil and 0.375 g of active ingredient B with 15 g of talc per pot with 750 cm³ of soil.

Preparation	Active ingredient per pot	Duration of action before infection	Attack quotient as % of attack
A	0.06 g = 0.0135%	24 h	12
	0.06 g	7 days	1
	0.06 g	15 days	0
	0.06 g	21 days	0
B	0.375 g = 0.05%	15 days	3
	0.375 g	21 days	0
	0.375 g	27 days	7

C L A I M

Fungicidal agents, which are or which contain substituted polyhalogen-cyclopentenes with a general formula:

[see figure]

in which X represents fluorine, chlorine, bromine or iodine, R an alkyl, cycloalkyl or araliphatic residue, possibly substituted by halogen or other heteroatoms and Y signifies R, X or hydrogen.

Brussels, 6 December 1961

(Signature)

p.p. J. Bede